REMARKS

Claims 1-19 and 32 are currently pending. Applicants affirm that, in response to a restriction requirement, Group 1 (claims 1-20) was elected, with traverse, and apologize that the response paper was inadvertently submitted unsigned. Claims 21-31, withdrawn pursuant to the restriction requirement, are cancelled, without prejudice to the prosecution of their subject matter in other patent applications. The claims are amended, and new claim 32 is added, and are supported by the original claims and the specification, particularly at page 16, line 29 continuing to page 17, line 4; page 17, lines 16-25; and page 63, lines 1-30.

The Examiner has provisionally rejected claims 1-20 under 35 U.S.C. § 101 as claiming the same invention of copending Application No. 10/971,483. The Examiner has rejected claims 12, 13 and 18 under 35 U.S.C. § 101 as directed toward non-statutory subject matter. The Examiner has rejected claims 1-6, 8-11, 14, 15, 17 and 19 under 35 U.S.C. § 112, first paragraph, as being unenabled. Furthermore, the Examiner has rejected claims 1-3, 5, 7, 12, 14, 16 and 18 under 35 U.S.C. § 102(b) as being anticipated by Angelastro et al. (Angelastro et al., 2000, Identification of diverse nerve growth factor-regulated genes by serial analysis of gene expression (SAGE) profiling, Proc. Natl. Acad. Sci. U.S.A. 97(19):10424-9) ("Angelastro et al."). For the reasons detailed below, the rejections should be withdrawn and the claims should be allowed to issue.

1. The Double Patenting Rejection

The Examiner has provisionally rejected claims 1-20 under 35 U.S.C. § 101 as claiming the same invention as that of claims 3-22 of copending Application No. 10/971,483.

Applicants respond, in response to a restriction requirement issued April 10, 2006 in copending Application 10/971,483, Applicants in that case elected to pursue claims 1 and 24, so that the claims at issue, 3-22, are effectively withdrawn from consideration. It is therefore requested that this rejection be deferred pending cancellation of claims 3-22 in United States Serial No. 10/971,483.

2. The Claims Are Directed To Statutory Subject Matter

The Examiner has rejected claims 12, 13 and 18 under 35 U.S.C. § 101 as directed toward non-statutory subject matter. The Examiner contends that the claims are drawn to "a differentiated neural cell" and "a population of cells.". The Examiner states that the cells can be in humans, and claims reading on *in vivo* human tissue, according to the examiner, are non-statutory because the claims read on part of a living human being *in situ*.

Applicants submit that the presently amended claims read upon statutory subject matter. As recommended by the Examiner, Applicants have amended the claims to recite "an isolated differentiated neural cell..." and "an isolated population of cells..." Since the presently amended claims are drawn to statutory subject matter, Applicants request that the rejection be withdrawn.

3. The Claims Are Enabled

A. Claims 6, 8-11, 15, 17 And 19 Are Enabled

The Examiner has rejected claims 6, 8-11, 15, 17 and 19 under 35 U.S.C. § 112, first paragraph, as being unenabled. The Examiner contends that the claims are directed to subject matter in which the present invention is used *in vivo*, and that such uses are not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which it is most nearly connected, to make and/or use the invention.

The Examiner contends that the claims are drawn to a large group of ATF5 inhibitors along with a large number of neurodegenerative disorders. According to the Examiner, the field of stem cell therapy is a "baby-science" with multiple art-recognized problems that must be overcome prior to the application of widespread therapies to neurodegenerative disorders. The Examiner further asserts that the field of gene therapy combined with stem cell therapy is poorly developed, and impeded by obstacles such as gene transfer efficiency, vector design, and regulatory issues which all pose multiple hurdles that must be resolved prior to their effective use. The Examiner also contends that human responses to these therapies, such as those using viral-based therapies, are harder to predict than animal responses. As such, according to the Examiner, it is difficult to make solid predictions on the likelihood of success with these therapies. Additionally, the Examiner contends that the art in the field of stem cell therapy for neurodegenerative disease or trauma is unpredictable in areas such as efficacy of stem cell delivery, differentiation, and the persistence of the cells in the diseased area. According to the Examiner, the level of skill in the art is low because Applicants have not reduced the claimed method to practice. The Examiner asserts that Applicants have not provided a working example demonstrating the treatment of nervous tissue degeneration in a

subject by inducing the differentiation of neural stem cells by inhibiting ATF5 *in vivo*, or by introducing cells differentiated *in vitro* into a subject in need of treatment. As such, the Examiner states that a skilled artisan would need to perform undue experimentation to practice the claimed invention.

Applicants assert that the specification enables one of ordinary skill in the art to practice the invention as claimed. The specification provides working examples which illustrate that the claimed methods can successfully induce neural differentiation. In particular, at page 63, lines 1-30, Applicants demonstrate that the *in vitro* inhibition of ATF5 in neural progenitor cells with dominant negative ATF5 (NTAzip-ATF5), or siRNA directed toward ATF5, accelerates neurogenesis in the neuronal progenitors by specifically interfering with the function of endogenous ATF5.

First, with regard to claims 8-11 and 17, the method of inducing differentiation recited in independent base claims 1 and 14 is achieved *in vitro*, and transplantation of the cells is an intended use for which no threshold goal is specified. There is no reason to predict that differentiation of the cell, once transplanted, will be reversed, or if so, in what time frame, so that transplantation of a differentiated neural cell will confer some benefit, either therapeutic, or as a research model. Therefore, these claims have two aspects - inducing differentiation *in vitro*, which the Examiner acknowledges is enabled, and transplantation of cells, which can be achieved using standard surgical techniques. Accordingly, Applicants assert that the claimed subject matter is, indeed, enabled by the specification.

With regard to claims 6 and 15, wherein a neuron *in vivo* is contacted with an ATF5 inhibitor, Applicants assert that the use of ATF5 specific agents such as RNAi, antisense RNA, or a dominant negative ATF5, to name a few, is within the capabilities of the person

skilled in the art. These techniques are accepted modes of nucleic acid delivery that the biotechnology industry continues to endorse.

Like claims 8-11 and 17, claim 19 similarly provides for differentiation *in vitro* followed by transplantation, but in the preamble establishes the objective of the claimed method as a means to treat nervous system degeneration in a subject. Because claim 19 lists a specific set of ATF5 inhibitors which belong to classes of agents which are regarded as having therapeutic benefit, as evidenced by the continued interest of the biotechnology industry, Applicants believe that claim 19 is enabled by the specification.

As noted by the Examiner, obstacles and hurdles exist for the application of widespread neurodegenerative disorder therapies. That said, however, Applicants submit that it is unnecessary to demonstrate therapeutic success of the claimed invention in human trials (see M.P.E.P § 2107.03(IV); and *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325(CCPA 1956) ("The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it.")). As such, Applicants assert that the presently amended claims are fully enabled by the specification, and therefore request that the rejection be removed.

B. Claims 1-5 And 14 Are Enabled

The Examiner has rejected claims 1-5 and 14 under 35 U.S.C. § 112, first paragraph, as being unenabled. The Examiner contends that these claims, which encompass both *in vitro* and *in vivo* applications, contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which it is most nearly connected, to make and/or use the invention, for reasons similar to those set forth

with regard to claims specifically directed to *in vivo* uses, discussed in the preceding section. The Examiner acknowledges that the *in vitro* uses are enabled.

In response, first, Applicants assert that it is not necessary for all embodiments falling within the scope of the claim be enabled. For almost any claimed method, there could be unrecited conditions that would preclude successful practice of the claim. For this reason alone, the rejection should be withdrawn.

Second, for reasons set forth above, Applicants assert that the practice of the invention *in vivo* is, in fact, enabled by the specification. The specification provides working examples which show that the claimed methods practiced on neuronal stem cells and progenitors *in vitro* demonstrate effectiveness *in vivo* because said cultured neurons are accepted model systems for neurons *in vivo*. For this reason, and other reasons set forth with regard to the preceding rejection, *in vivo* uses are enabled.

Accordingly, for all the foregoing reasons, the rejection should be withdrawn.

The Claims are Novel

The Examiner has rejected claims 1-3, 5, 7, 12, 14, 16 and 18 under 35 U.S.C. § 102(b) as being anticipated by Angelastro et al. The Examiner contends that Angelastro et al. describes the induction of neural differentiation in undifferentiated pheochromocytoma (PC12) cells after treatment with nerve growth factor (NGF). The Examiner further contends that Angelastro et al. teaches serial analysis of gene expression (SAGE) on the differentiating cells to determine any changes in gene expression resulting from NGF exposure. According to the Examiner, Angelastro et al. further discloses that ATF5 exhibits a decrease in expression as a

result of NGF exposure. The Examiner therefore contends that Angelastro et al. anticipates the above-listed claims.

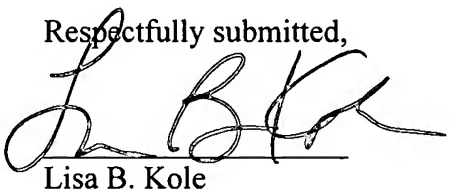
Applicants assert that the presently amended claims are novel and address the Examiner's rejection. The amended claims encompass a method of promoting neural differentiation of a neural progenitor cell by inhibiting ATF5 with an ATF5-specific inhibitor. Applicants submit that Angelastro et al. does not promote neural differentiation through the specific inhibition of ATF5. As stated by the Examiner, Angelastro et al. incubates PC12 cells with NGF to promote neural differentiation, and performs SAGE analysis to determine changes in gene expression following NGF incubation. As demonstrated by a class of genes that exhibit an increase in expression following NGF exposure, and a class of genes exhibiting a decrease in gene expression following NGF exposure (see page 10426, column 1, second paragraph; and table 1), NGF is not specific for ATF5. In fact, Angelastro et al. teaches a non-specific global affect on the NGF exposed cells wherein numerous genes may experience an increase or decrease in expression. The invention as claimed reads on the inhibition of ATF5 with an inhibitor that is specific for ATF5, and not a non-specific gene expression suppressor such as Angelastro et al.'s NGF. The claims are therefore novel and not anticipated by Angelastro et al.

CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicants believe that the invention described and defined by amended claims 1-20 are in condition for allowance. Withdrawal of all rejections and reconsideration of the amended claims is requested. An early allowance is earnestly sought.

Applicants believe that no additional fees are due in the timely filing of this response. In the event that fees are due, or overpayment is made, however, the Director is hereby authorized to charge payment of any such fees, or to credit any overpayment, to Deposit Account No. 02-4377.

Respectfully submitted,



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Enclosures